

FILE 'REGISTRY' ENTERED AT 16:27:48 ON 10 AUG 2005  
E "4-HYDROXYTAMOXIFEN"/CN 25

L1 1 S E3

FILE 'MEDLINE' ENTERED AT 16:28:48 ON 10 AUG 2005

L2 0 S L1  
L3 666 S 4-HYDROXYTAMOXIFEN/CN  
L4 233739 S BREAST OR MAMMAR?  
L5 256821 S DENSITY  
L6 1500 S L5 (S) L4  
L7 2 S L6 AND L3

FILE 'CAPLUS' ENTERED AT 16:30:37 ON 10 AUG 2005  
S 4-HYDROXYTAMOXIFEN/CN

FILE 'REGISTRY' ENTERED AT 16:30:42 ON 10 AUG 2005  
L8 1 S 4-HYDROXYTAMOXIFEN/CN

FILE 'CAPLUS' ENTERED AT 16:30:43 ON 10 AUG 2005

L9 1273 S L8  
L10 101462 S BREAST OR MAMMAR?  
L11 358546 S DENSITY  
L12 235 S L10 (S) L11  
L13 1 S L12 AND L9  
L14 496119 S DENS?  
L15 949 S L14 AND L10  
L16 3 S L15 AND L9  
L17 659727 S CANCER? OR TUMOR? OR NEOPLAS?  
L18 73400 S L17 AND L10  
L19 73400 S L18 (S) L10  
L20 69226 S L17 (S) L10  
L21 493 S L20 AND L8  
L22 4 S L21 AND PERCUTAN?

FILE 'PCTFULL' ENTERED AT 16:35:38 ON 10 AUG 2005

L23 268 S HYDROXYTAMOXIFEN  
L24 88096 S CANCER? OR TUMOR? OR NEOPLAS?  
L25 34444 S BREAST OR MAMMAR?  
L26 26782 S L24 (S) L25  
L27 209738 S DENS?  
L28 15333 S L27 AND L26  
L29 118 S L28 AND L23  
L30 18 S L29 AND DENSE  
L31 111 S L29 AND DENSITY  
L32 1644 S L25 (S) DENSIT?  
L33 22 S L32 AND L23  
L34 10 S L33 NOT PY>2001  
L35 11391 S PERCUTAN?  
L36 17 S L35 AND L23  
L37 16 S L36 AND L26  
L38 11 S L37 AND DENSIT?  
L39 1 S L23/AB  
L40 5061 S TAMOXIFEN  
L41 25 S L40/TI  
L42 67 S L40/AB  
L43 70 S L42 OR L41  
L44 58 S L43 AND L26  
L45 6 S L44 AND PERCUTAN?  
L46 6 S L45 AND DENSIT?  
L47 1644 S DENSIT? (S) L25  
L48 2 S L47 AND L46

CCESSION NUMBER: 1985:620824 CAPLUS  
 DOCUMENT NUMBER: 103:220824  
 TITLE: Antiestrogen drug for **percutaneous**  
 administration  
 INVENTOR(S): Mauvais Jarvis, Pierre; Kuttenn, Frederique  
 PATENT ASSIGNEE(S): Fr.  
 SOURCE: PCT Int. Appl., 15 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: French  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8503228	A1	19850801	WO 1984-EP436	19841221
W: DK, JP, US				
RW: AT, BE, CH, DE, FR, GB, LU, NL, SE				
FR 2558373	A1	19850726	FR 1984-927	19840120
FR 2558373	B1	19870703		
EP 151326	A1	19850814	EP 1984-201920	19841219
EP 151326	B1	19890712		
R: IT				
EP 169214	A1	19860129	EP 1985-900469	19841221
EP 169214	B1	19920311		
R: AT, BE, CH, DE, FR, GB, LI, LU, NL, SE				
JP 61500914	T2	19860508	JP 1985-500495	19841221
JP 06067826	B4	19940831		
AT 73334	E	19920315	AT 1985-900469	19841221
US 4919937	A	19900424	US 1985-777786	19850913
DK 8504203	A	19850917	DK 1985-4203	19850917
DK 155143	B	19890220		
DK 155143	C	19890703		
PRIORITY APPLN. INFO.:			FR 1984-927	A 19840120
			EP 1985-900469	A 19841221
			WO 1984-EP436	W 19841221

ACCESSION NUMBER: 2004087123 PCTFULL ED 20041019 EW 200442  
 TITLE (ENGLISH): PREVENTION AND TREATMENT OF **BREAST**  
**CANCER WITH 4-HYDROXY TAMOXIFEN**  
 TITLE (FRENCH): PREVENTION ET TRAITEMENT DU CANCER DU SEIN A L'AIDE DE  
 4-HYDROXY TAMOXIFENE  
 INVENTOR(S): SALIN-DROUIN, Dominique, 32, rue des Gatines, F-91370  
 Verrieres-le-Buisson, FR;  
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 PATENT ASSIGNEE(S): LABORATOIRES BESINS INTERNATIONAL, 5, rue du Bourg  
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 AGENT: NARGOLWALLA, Cyra\$, Cabinet Plasseraud, 65/67, rue de  
 la Victoire, F-75440 Paris Cedex 09\$, FR  
 LANGUAGE OF FILING: English  
 LANGUAGE OF PUBL.: English  
 DOCUMENT TYPE: Patent  
 PATENT INFORMATION:

NUMBER	KIND	DATE
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WO 2004087123	A1	20041014

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR  
 CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID  
 IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD  
 MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD  
 SE SG SK SL SY TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA  
 ZM ZW

RW (ARIPO):

BW GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW

RW (EAPO):

AM AZ BY KG KZ MD RU TJ TM

RW (EPO):

AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU  
 MC NL PT RO SE SI SK TR

RW (OAPI):

BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.:

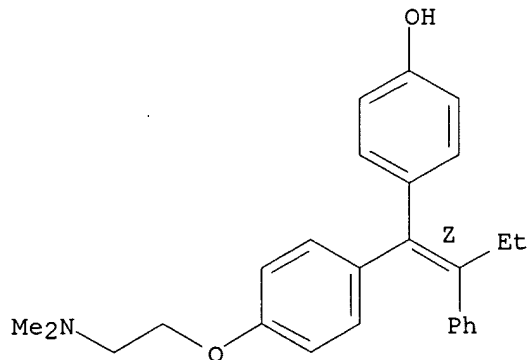
WO 2003-EP15029 A 20031215

PRIORITY INFO.:

US 2003-60/458,963 20030401

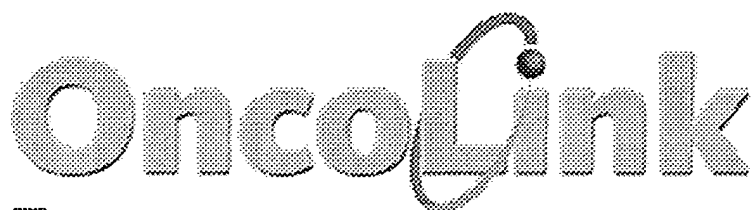
L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN  
 RN 68047-06-3 REGISTRY  
 CN Phenol, 4-[(1Z)-1-[4-[2-(dimethylamino)ethoxy]phenyl]-2-phenyl-1-butenyl]-  
 (9CI) (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN Phenol, 4-[1-[4-[2-(dimethylamino)ethoxy]phenyl]-2-phenyl-1-butenyl]-,  
 (Z)-  
 OTHER NAMES:  
 CN (Z)-4-Hydroxytamoxifen  
 CN **4-Hydroxytamoxifen**  
 CN 4-[(1Z)-1-[4-[2-(dimethylamino)ethoxy]phenyl]-2-phenyl-1-butenyl]phenol  
 CN Hydroxytamoxifen  
 CN ICI 79280  
 CN trans-4-Hydroxytamoxifen  
 CN trans-Hydroxytamoxifen  
 FS STEREOSEARCH  
 DR 65213-48-1, 72732-26-4, 76276-99-8  
 MF C26 H29 N O2  
 CI COM  
 LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS,  
 BIOTECHNO, CA, CAPLUS, CASREACT, CEN, CHEMCATS, CIN, CSCHEM, DDFU,  
 DRUGU, EMBASE, IMSDRUGNEWS, IPA, NIOSHTIC, PHAR, PROMT, RTECS\*,  
 TOXCENTER, USPAT2, USPATFULL  
 (\*File contains numerically searchable property data)  
 DT.CA Caplus document type: Conference; Dissertation; Journal; Patent  
 RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study);  
 FORM (Formation, nonpreparative); PREP (Preparation); PROC (Process);  
 PRP (Properties); RACT (Reactant or reagent); USES (Uses)  
 RLD.P Roles for non-specific derivatives from patents: BIOL (Biological  
 study); PREP (Preparation); PROC (Process); USES (Uses)  
 RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological  
 study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP  
 (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or  
 reagent); USES (Uses)  
 RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical  
 study); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation);  
 PROC (Process); PRP (Properties); USES (Uses)


Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1268 REFERENCES IN FILE CA (1907 TO DATE)  
 35 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 1273 REFERENCES IN FILE CAPLUS (1907 TO DATE)



 Abramson Cancer Center of the University of Pennsylvania

## Tamoxifen reduces mammographic breast density

Reuters Health

Posting Date: April 28, 2004

Last Modified: November 1, 2001

*Last Updated: 2004-04-28 13:21:39 -0400 (Reuters Health)*

NEW YORK (Reuters Health) - Mammographic breast density -- a risk factor for breast cancer -- is reduced in healthy women being treated with tamoxifen because of an increased risk of breast cancer, UK researchers report in the April 21st issue of the Journal of the National Cancer Institute.

This finding, lead investigator Dr. Jack Cuzick told Reuters Health "has important implications clinically. Firstly, it shows that breast density is a modifiable risk factor, strengthening its importance as a measure related to the hormonal milieu. Secondly, it suggests that changes in breast density may be useful as a surrogate for the effectiveness of preventive interventions, thus allowing a more rapid assessment of their effectiveness."

Dr. Cuzick of the Wolfson Institute of Preventative Medicine, London, and colleagues note that it is known that tamoxifen reduces breast density in women with breast cancer and that high breast density is a risk factor for cancer. However, tamoxifen's effect on breast density in healthy women and its effect on breast cancer risk are unclear.

To investigate, the researchers followed 818 healthy women who were involved in a placebo-controlled trial of tamoxifen for breast cancer prevention. All had at least twice the population risk of developing breast cancer because of factors such as a family history of the condition or benign proliferative breast disease.

At baseline, mammographic breast density was similar in tamoxifen and placebo patients. At 18 months, breast density had fallen by 7.9% in the tamoxifen group and 3.5% in the placebo group. This reduction continued for a total of 54 months. At that point breast density had fallen by 13.7% in the tamoxifen group and 7.3% in placebo patients.

The tamoxifen-associated breast density reduction was apparent in all subgroups, but was significantly affected by age. In those aged 45 years or less at study entry, the net reduction with tamoxifen was 13.5%. However, in women over the age of 55 years, it was 1.1%.

Whether the density reduction is reversed on tamoxifen cessation and whether, at an individual level, density reduction associated with a reduced risk of cancer requires further research, the team concludes.

J Natl Cancer Inst 2004;96:621-628.

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